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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
LI, BAO Q	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 07/06/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/649,480	STEGMANN ET AL.	
	Examiner	Art Unit	
	Bao Qun Li	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04/18/2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-34 and 36* is/are pending in the application.

4a) Of the above claim(s) *16, 18-19* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15,17,20-34 and 36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of group I, within the scope of species of SEQ ID NO: 7 in the reply filed on April 18, 2005 is acknowledged. The traversal is on the ground(s) that the species election is made with traverse since specie F of SEQ ID NO: 6 is the nucleic acid sequence of elected amino acid sequence of SEQ ID NO: 7.

2. Applicants' argument has been fully considered. The species F is rejoined with species G of SEQ ID NO: 7. To the context, the elected group I that reads on the elected species G and F are claims 2-15, 17, 20-34 and 36. Because claim 1 is linking claim. Therefore, claims 1-15, 17, 20-34 and 36 are considered before the examiner. Claims 16, 18 and 19 are withdrawn from consideration.

3. It should be noted that claims 1-34 and 36 are drafted as a method of using product by a process. MPEP 2113 cites: "[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985) (citations omitted).

4. To this context, the prior art rejections are applied as following:

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 1, 3-11, 13-15 are rejected under 35 U.S.C. 102(b) as being anticipated by Pu et al. (Circulation 1993, Vol. 88, No. 1, pp. 208-215).

7. Pu et al. teach a method of revascularization in the ischemic rabbit limb comprising to apply endothelial cell growth factor (ECGF, which is a synonym of FGF) to the ischemic limb area. The treatment significantly accelerates the revascularization in the ischemic limbs (See abstract and Figs. 1-5). Therefore, the claimed invention is anticipated by the cited references.

8. Claims 1, 3-11, 13-15 are rejected under 35 U.S.C. 102(b) as being anticipated by Banai et al. (Cir. Res. 1991, Vol. 69, No. 1, pp. 76-85).

9. Banai et al. disclose a method for improving blood circulation in an experimental ischemic myocardium comprising administration of acidic fibroblast growth factor (FGF-a) onto the myocardium of the dogs experimentally suffered from ischemic myocardial infarctions. They have demonstrated that FGF-a stimulates a striking smooth muscle cell hyperplasia in all arteries and small arteries exclusively in area of subendocardial infarctions, and administration of FGF-a into the myocardium of the dogs compromises the reduced coronary flows in the ischemic area because the FGF-stimulates vascularization of all smooth muscle cells in the ischemic areas (See abstract and Figs. 1-8). Therefore, the claimed invention is anticipated by the cited reference.

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

11. Claims 1, 3-11, 13-15, 20-22, 33 and 36 are rejected under 35 U.S.C. 102(a) as being anticipated by Schumacher et al. (Circulation, Feb, 1998, Vol. 97, pp. 645-650).

12. Schumacher et al. disclose a method for inducing a revascularization in ischemic myocardium by human acidic growth factor (FGF-1). The method comprises preparation of pharmaceutical composition comprising a human FGF-1 expressed by apathogenic strain E Coli carrying a plasmid encoding the genetic information of human FGF-1, and injection of the composition directly into the myocardium distal to the internal mammary

artery (IMA) and left anterior descending coronary artery (LAD) anastomosis and close to the LAD during the open heart venous bypass surgery at the concentration about 10 μg/kg body weight. They have demonstrated that the administration of the human FGF-1 into the ischemic myocardium region induces a significantly revasculation of the blood vessel in compared with the negative control. They concluded that neoanggiogenesis induced by human FGF-1 opens up a new possibilities for treating ischemic myocardial diseases (See entire document, especially, see pages 645, 646 , Figs. 4-8 and page 650). Therefore, the disclosure of Schumacher et al. anticipates the claims 1, 3-11, 13-15, 20-22, 33 and 36.

13. Claims 1, 3-11, 13-15 are rejected under 35 U.S.C. 102(a) as being anticipated by Htun et al. (J. Mol. Cell. Cardiol. April 1998, Vol. 30, pp. 867-877) in light of the disclosure of Battegay E.J. (Mol. Med. 1995, Vol. 73, pp. 333-346).

14. Htun et al. teach a method of treating or preventing pig myocardium suffered ischemic damage. The method comprises administering directly the human recombinant FGF-1 or FGF-2 into the myocardium via a direct intramyocardium infusion. While, the reference is silence about how does FGF-1 improve and protect the myocardial infusion, the mechanism of the FGF-1 for improving or preventing the myocardial infarction via stimulating the endothelial cells to form new blood vessels is well known in the art in light of the disclosure of Battegay. E.J. (See 336 and 338). Therefore, the claimed invention is anticipated by the cited reference.

Claim Rejections - 35 USC § 103

Claims 1, 3-11, 13-15, 20-22, 33 and 36 are rejected under 35 U.S.C. 102(b) as

15. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

16. Claims 1-15, 17, 20-34, and 36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schumacher et al. (Circulation, Feb, 1998, Vol. 97, pp. 645-650) for claims 1, 3-11, 13-15, 20-22, 33 and 36, Jaye et al. (US Patent No. 5,571,790A) and Fasol et al. (J. Thorac Cardiovasc. Surg. 1994, Vol. 107, pp. 1432-1439).

17. Claimed invention is directed to a method for revasculating an ischemic region comprising preparing a pharmaceutical composition comprising a recombinant fibroblast growth factor-1 (FGF-1), pharmaceutical fibrin glue and heparin and injecting an amount of said composition into the ischemic region during the open heart surgery, such as coronary artery bypass graft, wherein the ischemic region comprising at least one site of a heart wall.

18. Schumacher et al. disclose a method for induction of neoangiogenesis in ischemic myocardium by human acidic growth factor (FGF-1) comprising preparation of pharmaceutical composition comprising a human FGF-1 expressed by apathogenic strain E Coli that carries a plasmid encoding the genetic information of human FGF-1, and injection of the composition directly into the myocardium distal to the internal mammary artery (IMA) and left anterior descending coronary artery (LAD) anastomosis and close to the LAD, during the open heart venous bypass surgery at the concentration about 10 μg/kg body weight. They have demonstrated that the administration of the human FGF-1 into the ischemic myocardium region induce the significantly revasculation of the blood vessel in compared with the negative control. They concluded that neoanggiogenesis induced by human FGF-1 open s up new possibilities for treatment of ischemic myocardiadial disease (See entire document, especially, see pages 645- 646 , Figs. 4-8 and page 650). Schumacher et al. does not teach the nucleic acid and amino acid sequence of human FGF-1. Schumacher et al. do not teach that the composition comprising physiological fibrin glue and heparin, Schumacher et al. also lack of disclosure of the precise nucleic acid sequence and amino acid sequence of FGF-1.

19. Fasol. Et al. teach a method of using heparin-binding growth factor (HBGF) or α and β endothelial cell growth factors (α and β ECGF) (synonym of FGF) for inducing site directed angiogenesis in animal model comprises administering a composition comprising a recombinant HBGF or α or β ECGF in combinations with fibrin and

heparin into the hear wall during the surgical experiments. They teach a similar surgical procedure for the open hear surgery comprising making a thoracotomy incision, accessing to the myocardium of the left ventricle via a small incision into the pericardium, and placing the composition to the left ventricular myocardium. They found that the administration of the composition comprising FGF induce a significant blood vessel growth and addition of fibrin glue in the composition meets the conditions of being an easily available substance for applying the angiogenesis growth factor to the target organ, which has the conditional advantage of clinical applicability (See pages 2-3, 4-5, Fig. 4, pages 7-10).

20. Jaye et al. disclose the exactly same human FGF-1 (HECGF) polypeptide sequence and c DNA encoding such polypeptide, which has 100% identical to the amino acid sequences of claimed human FGF-1 DNA and amino acid sequences as claimed drafted (In fact, HECGF is an synonym of FGF). In addition, Jaye et al. explicitly teach that the human ECGF can be generated by the recombinant DNA technique also, and that the function of HEDF is to treat the damaged blood vessels (See claims 1-18).

21. Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention was filled to be motivated by the recited references and to treat ischemic tissue injury in view of the disclosures by Schumacher et al. Fasol et al. and Jaye et al. Because the suitable composition for treating the ischemic tissue or organ is already well described by Schumacher et, Fasol et al. and Jaye. Moreover, all three references teach that the function of FGF-1 is to induce angiogenesis of endothelial cell growth and a new blood vessel growth and development. Schumacher et al. and Fasol et al. particularly disclose that human FGF can be used in vivo or even for patients to improve the ischemic region blood circulation when it is applied to the ischemic region during the open heart coronary bypass operation. Hence the claimed invention as a whole is prima facie obvious absence unexpected results.

22. Regarding to the limitations of some procedure having product by process in claims 1-34 and 36, applicants' attention are further directed to the MPEP: which cites: The Patent Office bears a lesser burden of proof in making out a case of prima facie obviousness for product-by-process claims because of their peculiar nature"

than when a product is claimed in the conventional fashion. In re Fessmann, 489 F.2d 742, 744, 180 USPQ 324, 326 (CCPA 1974). Once the examiner provides a rationale tending to show that the claimed product appears to be the same or similar to that of the prior art, although produced by a different process, the burden shifts to applicant to come forward with evidence establishing an unobvious difference between the claimed product and the prior art product. In re Marosi, 710 F.2d 798, 802, 218 USPQ 289, 292 (Fed. Cir. 1983) (The claims were directed to a zeolite manufactured by mixing together various inorganic materials in solution and heating the resultant gel to form a crystalline metal silicate essentially free of alkali metal. The prior art described a process of making a zeolite which, after ion exchange to remove alkali metal, appeared to be "essentially free of alkali metal." The court upheld the rejection because the applicant had not come forward with any evidence that the prior art was not "essentially free of alkali metal" and therefore a different and unobvious product.). Ex parte Gray, 10 USPQ2d 1922 (Bd. Pat. App. & Inter. 1989) (The prior art disclosed human nerve growth factor (b-NGF) isolated from human placental tissue. The claim was directed to b-NGF produced through genetic engineering techniques. The factor produced seemed to be substantially the same whether isolated from tissue or produced through genetic engineering. While the applicant questioned the purity of the prior art factor, no concrete evidence of an unobvious difference was presented. The Board stated that the dispositive issue is whether the claimed factor exhibits any unexpected properties compared with the factor disclosed by the prior art. The Board further stated that the applicant should have made some comparison between the two factors to establish unexpected properties since the materials appeared to be identical or only slightly different.).

23. THE USE OF 35 U.S.C. 102 /103 REJECTIONS FOR PRODUCT-BY-PROCESS CLAIMS HAS BEEN APPROVED BY THE COURTS "[T]he lack of physical description in a product-by-process claim makes determination of the patentability of the claim more difficult, since in spite of the fact that the claim may recite only process limitations, it is the patentability of the product claimed and not

of the recited process steps which must be established. We are therefore of the opinion that when the prior art discloses a product which reasonably appears to be either identical with or only slightly different than a product claimed in a product-by-process claim, a rejection based alternatively on either section 102 or section 103 of the statute is eminently fair and acceptable. As a practical matter, the Patent Office is not equipped to manufacture products by the myriad of processes put before it and then obtain prior art products and make physical comparisons therewith." In re Brown, 459 F.2d 531, 535, 173 USPQ 685, 688 (CCPA 1972)

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bao Qun Li whose telephone number is 571-272-0904. The examiner can normally be reached on 7:00 am to 3:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 571-272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Bao Qun Li M.D.

06/24/2005